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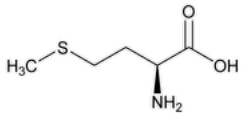
Methionine



$C_5H_{11}NO_2S$ 149.21

L-Methionine CAS RN®: 63-68-3; UNII: AE28F7PNPL.

DEFINITION

Methionine contains NLT 98.5% and NMT 101.5% of L-methionine ($C_5H_{11}NO_2S$), calculated on the dried basis.

IDENTIFICATION

• **A. Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**

ASSAY

• **Procedure**

Sample: 140 mg of Methionine

Blank: Mix 3 mL of formic acid and 50 mL of glacial acetic acid.

Titrimetric system

(See *Titrimetry ⟨541⟩*.)

Mode: Direct titration

Titrant: 0.1 N perchloric acid VS

Endpoint detection: Potentiometric

Analysis: Dissolve the *Sample* in 3 mL of formic acid and 50 mL of glacial acetic acid, and titrate with the *Titrant*.

Calculate the percentage of L-methionine ($C_5H_{11}NO_2S$) in the portion of the *Sample* taken:

$$\text{Result} = \{[(V_S - V_B) \times N \times F]/W\} \times 100$$

V_S = *Titrant* volume consumed by the *Sample* (mL)

V_B = *Titrant* volume consumed by the *Blank* (mL)

N = actual normality of the *Titrant* (mEq/mL)

F = equivalency factor, 149.2 mg/mEq

W = *Sample* weight (mg)

Acceptance criteria: 98.5%–101.5% on the dried basis

IMPURITIES

• **Residue on Ignition ⟨281⟩:** NMT 0.4%

• **Chloride and Sulfate ⟨221⟩, *Chloride***

Standard solution: 0.50 mL of 0.020 N hydrochloric acid

Sample: 0.73 g of Methionine

Acceptance criteria: NMT 0.05%

• **Chloride and Sulfate ⟨221⟩, *Sulfate***

Standard solution: 0.10 mL of 0.020 N sulfuric acid

Sample: 0.33 g of Methionine

Acceptance criteria: NMT 0.03%

Change to read:

• **▲Iron ⟨241⟩, *Procedures, Procedure 1*▲ (CN 1-Jun-2023) :** NMT 30 ppm

• **Related Compounds**

Phosphoric acid solution: 23 g/L of phosphoric acid

Solution A: Acetonitrile, *Phosphoric acid solution*, and water (0.5:12.5:87)

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Solution B: Acetonitrile, *Phosphoric acid solution*, and water (47.5:12.5:40)

Mobile phase: Gradient elution. See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
6	100	0
50	0	100
60	0	100
70	100	0

System suitability solution: Transfer 5 mg each of USP L-Methionine RS and L-methionine sulfoxide to a 50-mL volumetric flask, and dissolve in and dilute with *Solution A* to volume.

Standard solution: 30 µg/mL of USP L-Methionine RS in *Solution A*

***N*-Acetyl-D,L-methionine standard solution:** 0.06 mg/mL of USP *N*-Acetyl-D,L-methionine RS in *Solution A*

Sample solution: 30 mg/mL of Methionine in *Solution A*

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 205 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 50 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for L-methionine and L-methionine sulfoxide are 1.0 and 0.5, respectively.]

Suitability requirements

Resolution: NLT 5.0 between L-methionine and L-methionine sulfoxide peaks

Analysis

Samples: *Standard solution*, *N-Acetyl-D,L-methionine standard solution*, and *Sample solution*

Calculate the percentage of *N*-acetyl-D,L-methionine in the portion of Methionine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of *N*-acetyl-D,L-methionine from the *Sample solution*

r_S = peak response of *N*-acetyl-D,L-methionine from the *N-Acetyl-D,L-methionine standard solution*

C_S = concentration of USP *N*-Acetyl-D,L-methionine RS in the *N-Acetyl-D,L-methionine standard solution* (mg/mL)

C_U = concentration of Methionine in the *Sample solution* (mg/mL)

Separately calculate the percentage of methionine sulfoxide and any unspecified impurity in the portion of Methionine taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of methionine sulfoxide or any unspecified impurity from the *Sample solution*

r_S = peak response of methionine from the *Standard solution*

C_S = concentration of USP L-Methionine RS in the *Standard solution* (mg/mL)

C_U = concentration of Methionine in the *Sample solution* (mg/mL)

F = relative response factor (see *Table 2*)

Acceptance criteria: See *Table 2*. Disregard any impurities less than 0.05%.

Table 2

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Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Methionine sulfoxide	0.5	0.53	0.1
Methionine	1.00	—	—
N-Acetyl-D,L-methionine	3.4	—	0.2
Any unspecified impurity	—	1.0	0.1
Total unspecified impurities	—	—	0.30

SPECIFIC TESTS

- **Optical Rotation** ⟨781S⟩, *Procedures*, *Specific Rotation*
  Sample solution: 20 mg/mL in 6 N hydrochloric acid
  Acceptance criteria: +22.4° to +24.7°
- **pH** ⟨791⟩
  Sample solution: 10 mg/mL of solution
  Acceptance criteria: 5.6–6.1
- **Loss on Drying** ⟨731⟩
  Analysis: Dry at 105° for 3 h.
  Acceptance criteria: NMT 0.3%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in well-closed containers.
- **USP Reference Standards** ⟨11⟩
  USP *N*-Acetyl-D,L-methionine RS
  USP L-Methionine RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
METHIONINE	Fatkhulla K Tadjimukhamedov Associate Scientific Liaison	NBDS2020 Non-botanical Dietary Supplements

Chromatographic Database Information: Chromatographic Database

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